Assay Development for High Throughput Molecular Screening

RFA Number: RFA-RM-05-011

Part I Overview Information

Department of Health and Human Services

Participating Organizations
National Institutes of Health (NIH), (http://www.nih.gov)

Components of Participating Organizations
This RFA is developed as an NIH roadmap initiative (http://nihroadmap.nih.gov). All NIH Institutes and Centers participate in roadmap initiatives. The RFA will be administered by the National Institute of Neurological Disorders and Stroke (NINDS) on behalf of the NIH.

Announcement Type
Reissue for FY2005 of RFA-RM-04-012.

Catalog of Federal Domestic Assistance Number(s)
93.853

Key Dates

Release Date: December 7, 2004
Letters of Intent Receipt Date(s): January 31, 2005
Application Receipt Dates(s): February 14, 2005
Peer Review Date(s): June/July 2005
Council Review Date(s): September 2005
Earliest Anticipated Start Date: September 30, 2005
Additional Information To Be Available Date (Url Activation Date): Not Applicable
Expiration Date: February 15, 2005

Due Dates for E.O. 12372
Not Applicable

Executive Summary

- The purpose of this RFA is to facilitate the discovery of new molecular probes for investigating biological function by funding the development and adaptation of biological assays for automated high throughput molecular screening (HTS). This is one component of the NIH Molecular Libraries and Imaging Roadmap Initiative (http://nihroadmap.nih.gov/molecularlibraries/index.asp).
- Approximately $4 million will be available for this RFA.
- The NIH anticipates making approximately 40 awards.
- Grant mechanisms for funding will be the R03 (up to $50,000, limited to 1 year) and the R21 (up to $125,000, limited to 1 year).
- Eligible organizations include for-profit or non-profit, public or private, and domestic or foreign institutions and organizations, as well as governmental units and agencies.
- Eligible principal investigators include any individual with the skills, knowledge and resources necessary to carry out the proposed research.
- Applicants may submit more than one application.
- Applications must be prepared using the PHS 398 application forms, available at http://grants.nih.gov/grants/funding/phs398/phs398.html. Additional instructions, found in Section IV below, should be followed for this RFA.

Telecommunications for the hearing impaired is available at: TTY 301-451-0088

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Part II - Full Text of Announcement

Section I. Funding Opportunity Description

1. Research Objectives

The purpose of this RFA is to facilitate the discovery of new molecular probes for investigating biological function by funding the development and adaptation of biological assays for automated high throughput molecular screening (HTS) of collections chemical compounds. This is one component of the NIH Molecular Libraries and Imaging Roadmap Initiative (http://nihroadmap.nih.gov/molecularlibraries/index.asp), a major NIH effort to broaden access to HTS technologies. Other components of this Roadmap Initiative will support automated molecular screening within the Molecular Libraries Screening Centers Network, the creation of a chemical compound library at the Molecular Libraries Small Molecule Repository, and the development of HTS-related technologies.

High throughput molecular screening (HTS) is the automated, simultaneous testing of thousands of distinct chemical compounds in models of biological mechanisms or disease. Active compounds identified through HTS can provide powerful research tools to elucidate biological processes, or can form the basis of therapeutics development programs. The immense potential of HTS to impact the understanding of biology and disease is largely untapped because access to automated screening facilities and large compound libraries is limited in academic, government and non-profit research sectors. The NIH Molecular Libraries Roadmap Initiative will provide unprecedented access to these resources and allow the broad application of HTS in NIH-supported research.

The goal of this RFA is to initiate a continuously evolving stream of scientifically and technologically outstanding assays that can be automated and used for screening small molecules within the Molecular Libraries Screening Centers Network. It is open to all areas of biological and biomedical research, with the goal of providing new ways to explore cellular function. Funding will be provided to enable investigators to develop promising assay protocols and transform them for automated screening by demonstrating the responsiveness and robustness required for use in HTS. Emphasis will be placed on assays based on targets, either cellular or molecular, for which an inadequate array of selective and potent small molecule modulators are available to the public.

Many of the in vitro models of biological mechanisms and disease that are used in low throughput studies, such as the effects of specific compounds or genetic perturbations, can be adapted to high throughput formats for the purpose of screening large compound collections. There are a number of characteristics that make an assay suitable for high throughput approaches. The assay must be robust, reproducible and have a readout that is amenable to automated analysis. In addition, it must be possible to miniaturize the assay to a 96-well or higher density format, and the assay protocol should be simple enough for automated handling. A broad range of models share these features, including biochemical assays, cellular models and certain model organisms such as yeast or C. elegans. This RFA will support the development of innovative assays for use both in basic research and in therapeutics development programs, with an emphasis on novelty of approach to biology or disease. Appropriate assays might include but are not limited to:

- Biochemical or cell-based assays of activity or interaction involving proteins and/or other biological molecules.
- Assays of cellular or molecular phenotypes.
- Modulation of expression of genes of interest, including effects on transcription, translation or RNA splicing
- Assays involving mutant proteins associated with disease.
- Cell-based assays of cell signaling or biosynthetic pathways.
- Assays using model organisms such as yeast or C. elegans.

Proposals should include plans to demonstrate assay reproducibility and feasibility for adaptation to an automated, high-throughput screening approach. The application should describe plans for demonstration of feasibility for HTS. These plans must include:

- Use of reagents and readouts that can be used in an automated HTS environment such as absorbance, fluorescence, luminescence, scintillation proximity assay (SPA), fluorescence resonance energy transfer (FRET), bioluminescence resonance energy transfer (BRET), biophysical readouts, and cell based imaging screens. Assays developed for HTS should be easy to automate and steps such as centrifugation, filtration and extraction should be avoided. Assays that require only addition of reagents, i.e. “mix and measure” assays, are preferable.
- A detailed proposal to demonstrate highly robust and reproducible behavior in a 96-well or higher density format (e.g., 384- or 1536-well plates). Generally, the assay protocol should demonstrate: 1) a signal of sufficient intensity that it can be easily measured from a microtitre plate in low volume, 2) a signal-to-background ratio of at least 5 and a coefficient of variation (CV) below 10% determined from measurements across the entire plate (these factors are typically expressed as the statistical parameter, Z', which has an acceptable lower limit of 0.5), 3) reproducible, dose-dependent

responses to pharmacological standards or other control conditions, 4) tolerance to the effect of DMSO at 0.1-1%. Between-plate and day-to-day variations also provide useful information on how well the assay will perform, as will the determination of reagent stability to storage and assay conditions.

The assay plan should include demonstration of selectivity and reproducibility of response to a small but diverse collection of at least several hundred compounds, such as a collection of FDA approved drugs or other bioactive molecules.

Although HTS with the assay is outside the scope of this RFA, the applicant must anticipate the use of the assay in a high throughput screen and provide a clear plan for evaluating the significance of active compounds obtained. The plan for future use of the assay will be considered in the peer review of the proposal. The plan must include counter-screens and secondary screens to rule out artifacts and prioritize active compounds for further testing. It is likely that a few hundred active compounds may be identified in a primary HTS effort; therefore the secondary screening plan should be feasible for the evaluation of hundreds of compounds.

The overall goals for the use of compounds identified in the proposed assay in an HTS effort should be well defined and clearly presented. This discussion should include the expected future use of the compounds in a follow-up research program, either in the context of biological research or therapeutics development.

A key goal of this RFA is to support the transition of established assays to an HTS format. Conversion of established assays to an HTS format will be supported by a 1 year R03 mechanism (up to $50,000 direct costs). The R03 mechanism is appropriate for assays that are well along in development, but that require demonstration of robustness and feasibility for use in HTS.

In addition, a limited number of projects to develop new assays will be funded through a 1 year R21 mechanism (up to $125,000 direct costs). Projects funded with the R21 mechanism will be highly innovative and have a reasonable chance of producing a viable HTS assay. Some degree of risk is acceptable, particularly if innovation is high, but the plans for demonstrating readiness for HTS under the award must be well defined in the application.

This RFA is intended to facilitate development and adaptation of screening assays to be considered for use within the NIH Roadmap Molecular Libraries Screening Centers Network (MLSCN). However, although assays developed under this RFA will be eligible for consideration by the NIH screening centers, funding under this RFA does not carry a commitment by NIH to accept the assay for screening within the MLSCN. The selection of fully developed assays for screening within the MLSCN will be done through a separate solicitation and review process. Grantees funded under the present RFA will be free to use their assays at screening facilities other than the MLSCN.

Please note that, although NINDS is coordinating the solicitation and review of applications for this RFA, this is an NIH-wide Roadmap initiative that will support all areas of NIH-sponsored research and reviewers will be selected with expertise appropriate to the breadth of applications received. Potential applicants to this RFA should also review the NIH Guide for other, Institute-specific announcements of programs for assay development and follow up.

See Section VIII, Other Information - Required Federal Citations, for policies related to this announcement.

Section II. Award Information

1. Mechanism(s) of Support

This funding opportunity will use a modified R03 mechanism (limited to 1 year, up to $50,000 direct costs) and a modified R21 mechanism (limited to 1 year, up to $125,000 direct costs). As an applicant, you will be solely responsible for planning, directing, and executing the proposed project.

This funding opportunity uses just-in-time concepts. It also uses the modular budget format described in the PHS 398 application instructions (see http://grants.nih.gov/grants/funding/modular/modular.htm).

2. Funds Available

- NIH expects to award $4 million through this announcement;
- NIH anticipates approximately 40 awards;
- Direct costs will awarded up to $50,000 (for R03s) and up to $125,000 (for R21s)
- the anticipated start date for these awards is September 30, 2005, with periods of performance for 1 year only.

NIH intends to commit approximately $4 million dollars in FY 05 to fund approximately 40 new and/or competing continuation grants in response to this RFA. An applicant may request a project period of up to 1 year and a budget for direct costs up to $ 50,000 for an R03 and $125,000 for an R21. Because the nature and scope of the proposed research will vary from application to application, it is anticipated that the size of each award will also vary. Although the financial plans of NIH provide support for this program, awards pursuant to this funding opportunity are contingent upon the availability of funds and the receipt of a sufficient number of meritorious applications.

Facilities and administrative costs requested by consortium participants are not included in the direct cost limitation, see NOT-OD-04-040.

Section III. Eligibility Information

1. Eligible Applicants

1.A. Eligible Institutions

You may submit (an) application(s) if your organization has any of the following characteristics:

- For-profit organizations
- Non-profit organizations
- Public or private institutions, such as universities, colleges, hospitals, and laboratories
- Units of State government
- Units of local government
- Eligible agencies of the Federal government
- Foreign Institutions
- Domestic Institutions
- Faith-based or community-based organizations

Applicants' failure to meet an eligibility criterion by the time of an application deadline will preclude NIH from making an award. Applications for renewal or supplementation of existing projects are eligible to compete with applications for new awards.

1.B. Eligible Individuals

Any individual with the skills, knowledge, and resources necessary to carry out the proposed research is invited to work with their institution to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH programs.

2. Cost Sharing or Matching

Cost sharing is not required.

The most current Grants Policy Statement can be found at:
http://grants.nih.gov/grants/policy/nihgps_2003/nihgps_Part2.htm#matching_or_cost_sharing.

3. Other-Special Eligibility Criteria

Relevance to the goals of the RFA described under Section I, Research Objectives, will be considered in accepting applications for review. Applications that do not meet the goal of developing and validating an assay for high throughput molecular screening will not be reviewed. Applicants may submit more than one application under this announcement.

Section IV. Application and Submission Information

1. Address to Request Application Information

The PHS 398 application instructions are available at http://grants.nih.gov/grants/funding/phs398/phs398.html in an interactive format. Applicants must use the currently approved version of the PHS 398. For further assistance contact GrantsInfo, Telephone (301) 435-0714, Email: GrantsInfo@nih.gov.

Telecommunications for the hearing impaired: TTY 301-451-0088.

2. Content and Form of Application Submission

Applications must be prepared using the most current PHS 398 research grant application instructions and forms. Applications must have a D&B Data Universal Numbering System (DUNS) number as the universal identifier when applying for Federal grants or cooperative agreements. The D&B number can be obtained by calling (866) 705-5711 or through the web site at http://www.dnb.com/us/. The D&B number should be entered on line 11 of the face page of the PHS 398 form.

The title and number of this funding opportunity must be typed on line 2 of the face page of the application form and the YES box must be checked.

Supplementary Instructions: Use the PHS 398 form with the following modifications:

For R03 applications, follow instructions at http://grants.nih.gov/grants/guide/pa-files/PA-03-108.html. For R21 applications, follow instructions at http://grants.nih.gov/grants/guide/pa-files/PA-03-107.html. The following exceptions to the general R03 and R21 instructions will apply for this RFA:

Research Plan: Items a - d of the Research Plan (Specific Aims, Background and Significance, Preliminary Studies, and Research Design and Methods) may not exceed a total of 10 pages for either the R03 or the R21 applications.

Appendix: Publications or other printed material should not be included in the appendix. The appendix may include original, glossy photographs or color images of data provided that a photocopy (may be reduced in size) is also included within the page limits of the research plan.

3. Submission Dates

Applications must be received on or before the receipt date described below (Section IV.3.A). Submission times N/A.

3.A. Receipt, Review and Anticipated Start Dates

Letter of Intent Receipt Date: January 31, 2005
Application Receipt Date(s): February 14, 2005
Peer Review Date: June/July 2005
Council Review Date: September 2005
Earliest Anticipated Start Date: September 30, 2005

3.A.1. Letter of Intent

Prospective applicants are asked to submit a letter of intent that includes the following information:

- Descriptive title of proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions
- Number and title of this funding opportunity

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows IC staff to estimate the potential review workload and plan the review.

The letter of intent is to be sent by the date listed at the beginning of this document.

The letter of intent should be sent to:

Jill Heemskerk, Ph.D.
Technology Development

NINDS
6001 Executive Boulevard
NSC, Room 2229
Bethesda, MD 20892
Telephone: (301) 496-1779
Email: heemskej@ninds.nih.gov

3.B. Sending an Application to the NIH

Applications must be prepared using the PHS 398 research grant application instructions and forms as described above. Submit a signed, typewritten original of the application, including the checklist, and three signed photocopies in one package to:

Center for Scientific Review
National Institutes of Health
6701 Rockledge Drive, Room 1040, MSC 7710
Bethesda, MD 20892-7710 (U.S. Postal Service Express or regular mail)
Bethesda, MD 20817 (for express/courier service; non-USPS service)

At the time of submission, two additional copies of the application must be sent to:

Chief, Scientific Review Branch
National Institute of Neurological Disorders and Stroke/NIH/DHHS
6001 Executive Boulevard, Room 3208
Bethesda, MD 20892 (Rockville, MD 20852 for overnight couriers)
Telephone: (301) 496-9223
Email: nindsreview.nih.gov@mail.nih.gov

Using the RFA Label: The RFA label available in the PHS 398 application instructions must be affixed to the bottom of the face page of the application. Type the RFA number on the label. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title and number must be typed on line 2 of the face page of the application form and the YES box must be marked. The RFA label is also available at: http://grants.nih.gov/grants/funding/phs398/labels.pdf. Personal deliveries of applications are no longer permitted.

3.C. Application Processing

Applications must be **received on or before the application receipt date(s)** described above (Section IV.3.A.). If an application is received after that date, it will be returned to the applicant without review. Upon receipt, applications will be evaluated for completeness by the CSR and responsiveness by the NINDS. Incomplete and non-responsive applications will not be reviewed.

The NIH will not accept any application in response to this funding opportunity that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. However, when a previously unfunded application, originally submitted as an investigator-initiated application, is to be submitted in response to a funding opportunity, it is to be prepared as a NEW application. That is, the application for the funding opportunity must not include an Introduction describing the changes and improvements made, and the text must not be marked to indicate the changes from the previous unfunded version of the application.

Although there is no immediate acknowledgement of the receipt of an application, applicants are generally notified of the review and funding assignment within eight (8) weeks.

4. Intergovernmental Review

This initiative is not subject to intergovernmental review.

5. Funding Restrictions

All NIH awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement. The Grants Policy Statement can be found at http://grants.nih.gov/grants/policy/policy.htm (see also Section VI.3. Award Criteria).

Pre-Award Costs are allowable. A grantee may, at its own risk and without NIH prior approval, incur obligations and expenditures to cover costs up to 90 days before the beginning date of the initial budget period of a new or competing

continuation award if such costs: are necessary to conduct the project, and would be allowable under the grant, if awarded, without NIH prior approval. If specific expenditures would otherwise require prior approval, the grantee must obtain NIH approval before incurring the cost. NIH prior approval is required for any costs to be incurred more than 90 days before the beginning date of the initial budget period of a new or competing continuation award.

The incurrence of pre-award costs in anticipation of a competing or non-competing award imposes no obligation on NIH either to make the award or to increase the amount of the approved budget if an award is made for less than the amount anticipated and is inadequate to cover the pre-award costs incurred. NIH expects the grantee to be fully aware that pre-award costs result in borrowing against future support and that such borrowing must not impair the grantee's ability to accomplish the project objectives in the approved time frame or in any way adversely affect the conduct of the project. See NIH Grants Policy Statement http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part6.htm.

6. Other Submission Requirements

Applications requesting up to $250,000 per year in direct costs must be submitted in a modular budget format. The modular budget format simplifies the preparation of the budget in these applications by limiting the level of budgetary detail. Applicants request direct costs in $25,000 modules. Section C of the research grant application instructions for the PHS 398 at http://grants.nih.gov/grants/funding/phs398/phs398.html includes step-by-step guidance for preparing modular budgets. Applicants must use the currently approved version of the PHS 398. Additional information on modular budgets is available at http://grants.nih.gov/grants/funding/modular/modular.htm.

Plan for Sharing Research Data

The precise content of the data-sharing plan will vary, depending on the data being collected and how the investigator is planning to share the data. Applicants who are planning to share data may wish to describe briefly the expected schedule for data sharing, the format of the final dataset, the documentation to be provided, whether or not any analytic tools also will be provided, whether or not a data-sharing agreement will be required and, if so, a brief description of such an agreement (including the criteria for deciding who can receive the data and whether or not any conditions will be placed on their use), and the mode of data sharing (e.g., under their own auspices by mailing a disk or posting data on their institutional or personal website, through a data archive or enclave). Investigators choosing to share under their own auspices may wish to enter into a data-sharing agreement. References to data sharing may also be appropriate in other sections of the application.

Applicants requesting more than $500,000 in direct costs in any year of the proposed research must include a plan for sharing research data in their application. The funding organization will be responsible for monitoring the data sharing policy (http://grants.nih.gov/grants/policy/data_sharing).

The reasonableness of the data sharing plan or the rationale for not sharing research data may be assessed by the reviewers. However, reviewers will not factor the proposed data sharing plan into the determination of scientific merit or the priority score.

Sharing Research Resources

NIH policy requires that grant awardee recipients make unique research resources readily available for research purposes to qualified individuals within the scientific community after publication (NIH Grants Policy Statement http://grants.nih.gov/grants/policy/nihgps_2003/index.htm and http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part7.htm#_Toc54600131). Investigators responding to this funding opportunity should include a plan for sharing research resources addressing how unique research resources will be shared or explain why sharing is not possible.

The adequacy of the resources sharing plan and any related data sharing plans will be considered by Program staff of the funding organization when making recommendations about funding applications. The effectiveness of the resource sharing will be evaluated as part of the administrative review of each non-competing Grant Progress Report (PHS 2590, http://grants.nih.gov/grants/funding/2590/2590.htm). See Section VI.3. Award Criteria.

Section V. Application Review Information

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1. Criteria

The following will be considered in making funding decisions:

- Scientific merit of the proposed project as determined by peer review
- Availability of funds
- Relevance of program priorities

2. Review and Selection Process

Upon receipt, applications will be reviewed for completeness by the CSR and responsiveness by the NINDS. Incomplete and/or non-responsive applications will not be reviewed.

Applications that are complete and responsive to the RFA will be evaluated for scientific and technical merit by an appropriate peer review group convened by NINDS in accordance with the review criteria stated below.

As part of the initial merit review, all applications will:

- Undergo a selection process in which only those applications deemed to have the highest scientific merit, generally the top half of applications under review, will be discussed and assigned a priority score.
- Receive a written critique.
- Receive a second level of review by the NINDS National Advisory Council.

The goals of NIH supported research are to advance our understanding of biological systems, to improve the control of disease, and to enhance health. In their written critiques, reviewers will be asked to comment on each of the following criteria in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals. Each of these criteria will be addressed and considered in assigning the overall score, weighting them as appropriate for each application. Note that an application does not need to be strong in all categories to be judged likely to have major scientific impact and thus deserve a high priority score. For example, an investigator may propose to carry out important work that by its nature is not innovative but is essential to move a field forward.

1. Significance. Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge or clinical practice be advanced? What will be the effect of these studies on the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field? Is there an adequate plan for evaluating the activities of the compounds identified in a high throughput screen, e.g., in secondary screens? Are there important and well-defined goals for the use of active compounds identified with the proposed assay, either as research tools or for therapeutics development?

2. Approach. Are the conceptual or clinical framework, design, methods, and analyses adequately developed, well integrated, well reasoned, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics? Is it feasible to adapt the proposed assay to a HTS format? Is it likely that the assay will produce reliable results in a high throughput screen?

3. Innovation. Is the project original and innovative? For example: Does the project challenge existing paradigms or clinical practice; address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools, or technologies for this area?

4. Investigators. Are the investigators appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and other researchers? Does the investigative team bring complementary and integrated expertise to the project (if applicable)?

5. Environment. Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed studies benefit from unique features of the scientific environment, or subject populations, or employ useful collaborative arrangements? Is there evidence of institutional support?

2.A. Additional Review Criteria:

In addition to the above criteria, the following items will continue to be considered in the determination of scientific merit and the priority score:

Protection of Human Subjects from Research Risk: The involvement of human subjects and protections from research risk relating to their participation in the proposed research will be assessed (see the Research Plan, Section E on Human Subjects in the PHS Form 398).

Care and Use of Vertebrate Animals in Research: If vertebrate animals are to be used in the project, the five items described under Section F of the PHS Form 398 research grant application instructions will be assessed.

2.B. Additional Review Considerations

Budget: The reasonableness of the proposed budget and the requested period of support in relation to the proposed research. The priority score should not be affected by the evaluation of the budget.

2.C. Sharing Research Data

Data Sharing Plan: The reasonableness of the data sharing plan or the rationale for not sharing research data may be assessed by the reviewers. However, reviewers will not factor the proposed data sharing plan into the determination of scientific merit or the priority score. The funding organization will be responsible for monitoring the data sharing policy. http://grants.nih.gov/grants/policy/data_sharing.

2.D. Sharing Research Resources

NIH policy requires that grant awardee recipients make unique research resources readily available for research purposes to qualified individuals within the scientific community after publication (See the NIH Grants Policy Statement http://grants.nih.gov/grants/policy/nihgps/part_ii_5.htm#availofrr and http://ott.od.nih.gov/newpages/rtguide_final.html). Investigators responding to this funding opportunity should include a sharing research resources plan addressing how unique research resources will be shared or explain why sharing is not possible.

The adequacy of the resources sharing plan will be considered by Program staff of the funding organization when making recommendations about funding applications. Program staff may negotiate modifications of the data and resource sharing plans with the awardee before recommending funding of an application. The final version of the data and resource sharing plans negotiated by both will become a condition of the award of the grant. The effectiveness of the resource sharing will be evaluated as part of the administrative review of each non-competing Grant Progress Report (PHS 2590). See Section VI.3. Award Criteria.

3. Anticipated Announcement and Award Dates

Not Applicable.

Section VI. Award Administration Information

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1. Award Notices

After the peer review of the application is completed, the Principal Investigator will also receive a written critique called a Summary Statement.

If the application is under consideration for funding, NIH will request "just-in-time" information from the applicant. For details, applicants may refer to the NIH Grants Policy Statement Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General (http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_part4.htm).

A formal notification in the form of a Notice of Grant Award (NGA) will be provided to the applicant organization. The NGA signed by the grants management officer is the authorizing document.

Selection of an application for award is not an authorization to begin performance. Any costs incurred before receipt of the NGA are at the recipient's risk. These costs may be reimbursed only to the extent considered allowable pre-award costs. See Also Section IV.5. Funding Restrictions.

The NGA will be sent by e-mail to the authorized business official at the grantee institution.

2. Administrative Requirements

All NIH grant and cooperative agreement awards include the NIH Grants Policy Statement as part of the notice of grant award. For these terms of award, see the NIH Grants Policy Statement Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General (http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part4.htm) and Part II Terms and Conditions of NIH Grant

Awards, Subpart B: Terms and Conditions for Specific Types of Grants, Grantees, and Activities (http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_part9.htm).

The following Terms and Conditions will be incorporated into the award statement and will be provided to the Principal Investigator as well as to the appropriate institutional official, at the time of award.

3. Award Criteria

Awardees will be required to submit the PHS Non-Competing Grant Progress Report, Form 2590 annually (http://grants.nih.gov/grants/funding/2590/2590.htm) and financial statements as required in the NIH Grants Policy Statement.

Section VII. Agency Contacts

We encourage your inquiries concerning this funding opportunity and welcome the opportunity to answer questions from potential applicants. Inquiries may fall into three areas: scientific/research, peer review, and financial or grants management issues:

1. Scientific / Research Contacts:

Jill Heemskerk, PhD
Technology Development
National Institute of Neurological Disorders and Stroke/NIH/DHHS
6001 Executive Boulevard, Room 2229
Bethesda, MD 20892 (20852 for overnight couriers)
Telephone: (301) 496-1779
Email: heemskej@ninds.nih.gov

2. Peer Review Contacts:

Chief, Scientific Review Branch
National Institute of Neurological Disorders and Stroke/NIH/DHHS
6001 Executive Boulevard, Room 3208
Bethesda , MD 20892 (20852 for overnight courier)
Telephone: (301) 496-9223
Email: nindsreview.nih.gov@mail.nih.gov

3. Financial or Grants Management Contacts:

Karen Walker
Grants Management Branch
National Institute of Neurological Disorders and Stroke/NIH/DHHS
6001 Executive Boulevard, Room 3248
Bethesda , MD 20892 (20852 for overnight courier)
Telephone: (301) 496-7359
Email: assaysgmb@mail.nih.gov

Section VIII. Other Information

Required Federal Citations

Use of Animals in Research:
Recipients of PHS support for activated involving live, vertebrate animals must comply with PHS Policy on Humane Care and Use of Laboratory Animals (http://grants.nih.gov/grants/olaw/references/PHSPolicyLabAnimals.pdf) as mandated by the Health Research Extension Act of 1985 (http://grants.nih.gov/grants/olaw/references/hrea1985.htm), and the USDA Animal Welfare Regulations (http://www.nal.usda.gov/awic/legislat/usdaleg1.htm) as applicable.

Human Subjects Protection:
Federal regulations (45CFR46) require that applications and proposals involving human subjects must be evaluated with reference to the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained (http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm).

Sharing Research Data:
Investigators submitting an NIH application seeking $500,000 or more in direct costs in any single year are expected to include a plan for data sharing or state why this is not possible (http://grants.nih.gov/grants/policy/data_sharing).

Investigators should seek guidance from their institutions, on issues related to institutional policies and local IRB rules, as well as local, State and Federal laws and regulations, including the Privacy Rule. Reviewers will consider the data sharing plan but will not factor the plan into the determination of the scientific merit or the priority score.

Sharing of Model Organisms:
NIH is committed to support efforts that encourage sharing of important research resources including the sharing of model organisms for biomedical research (see http://grants.nih.gov/grants/policy/model_organism/index.htm). At the same time the NIH recognizes the rights of grantees and contractors to elect and retain title to subject inventions developed with Federal funding pursuant to the Bayh Dole Act (see the NIH Grants Policy Statement http://grants.nih.gov/grants/policy/nihgps_2003/index.htm). All investigators submitting an NIH application or contract proposal, beginning with the October 1, 2004 receipt date, are expected to include in the application/proposal a description of a specific plan for sharing and distributing unique model organism research resources generated using NIH funding or state why such sharing is restricted or not possible. This will permit other researchers to benefit from the resources developed with public funding. The inclusion of a model organism sharing plan is not subject to a cost threshold in any year and is expected to be included in all applications where the development of model organisms is anticipated.

Required Education on the Protection of Human Subject Participants:
NIH policy requires education on the protection of human subject participants for all investigators submitting NIH applications for research involving human subjects and individuals designated as key personnel. The policy is available at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html.

Human Embryonic Stem Cells (hESC):
Criteria for federal funding of research on hESCs can be found at http://stemcells.nih.gov/index.asp and at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-005.html. Only research using hESC lines that are registered in the NIH Human Embryonic Stem Cell Registry will be eligible for Federal funding (http://escr.nih.gov/). It is the responsibility of the applicant to provide in the project description and elsewhere in the application as appropriate, the official NIH identifier(s) for the hESC line(s)to be used in the proposed research. Applications that do not provide this information will be returned without review.

Public Access to Research Data through the Freedom of Information Act:
The Office of Management and Budget (OMB) Circular A-110 has been revised to provide public access to research data through the Freedom of Information Act (FOIA) under some circumstances. Data that are (1) first produced in a project that is supported in whole or in part with Federal funds and (2) cited publicly and officially by a Federal agency in support of an action that has the force and effect of law (i.e., a regulation) may be accessed through FOIA. It is important for applicants to understand the basic scope of this amendment. NIH has provided guidance at http://grants.nih.gov/grants/policy/a110/a110_guidance_dec1999.htm. Applicants may wish to place data collected under this PA in a public archive, which can provide protections for the data and manage the distribution for an indefinite period of time. If so, the application should include a description of the archiving plan in the study design and include information about this in the budget justification section of the application. In addition, applicants should think about how to structure informed consent statements and other human subjects procedures given the potential for wider use of data collected under this award.

Standards for Privacy of Individually Identifiable Health Information:
The Department of Health and Human Services (DHHS) issued final modification to the "Standards for Privacy of Individually Identifiable Health Information", the "Privacy Rule", on August 14, 2002. The Privacy Rule is a federal regulation under the Health Insurance Portability and Accountability Act (HIPAA) of 1996 that governs the protection of individually identifiable health information, and is administered and enforced by the DHHS Office for Civil Rights (OCR).

Decisions about applicability and implementation of the Privacy Rule reside with the researcher and his/her institution. The OCR website (http://www.hhs.gov/ocr/) provides information on the Privacy Rule, including a complete Regulation Text and a set of decision tools on "Am I a covered entity?" Information on the impact of the HIPAA Privacy Rule on NIH processes involving the review, funding, and progress monitoring of grants, cooperative agreements, and research contracts can be found at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-025.html.

URLs in NIH Grant Applications or Appendices:
All applications and proposals for NIH funding must be self-contained within specified page limitations. Unless otherwise specified in an NIH solicitation, Internet addresses (URLs) should not be used to provide information necessary to the review because reviewers are under no obligation to view the Internet sites. Furthermore, we caution reviewers that their anonymity may be compromised when they directly access an Internet site.

Authority and Regulations:
This program is described in the Catalog of Federal Domestic Assistance at http://www.cfda.gov/ and is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review. Awards are made under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and under Federal Regulations 42 CFR 52 and 45 CFR Parts 74 and 92. All awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement. The NIH Grants Policy Statement can be found at http://grants.nih.gov/grants/policy/policy.htm.

The PHS strongly encourages all grant recipients to provide a smoke-free workplace and discourage the use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care, or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

Loan Repayment Programs:
NIH encourages applications for educational loan repayment from qualified health professionals who have made a commitment to pursue a research career involving clinical, pediatric, contraception, infertility, and health disparities related areas. The LRP is an important component of NIH's efforts to recruit and retain the next generation of researchers by providing the means for developing a research career unfettered by the burden of student loan debt. Note that an NIH grant is not required for eligibility and concurrent career award and LRP applications are encouraged. The periods of career award and LRP award may overlap providing the LRP recipient with the required commitment of time and effort, as LRP awardees must commit at least 50% of their time (at least 20 hours per week based on a 40 hour week) for two years to the research. For further information, please see: http://www.lrp.nih.gov/.

Weekly TOC for this Announcement
NIH Funding Opportunities and Notices

Department of Health and Human Services

National Institutes of Health (NIH)
9000 Rockville Pike
Bethesda, Maryland 20892

Animal Welfare Act and Regulations

Animal Welfare Information Center

United States Department of Agriculture
Agricultural Research Service
National Agricultural Library

- Questions & Answers about the Animal Welfare Act and Its Regulations for Biomedical Research Institutions [Full Text]

- Animal Welfare Act Interpretive Summaries [Full Text]

- Animal Welfare Act as Amended (7 USC, 2131-2159) [Full Text, Summary]

    - Public Law 89-544 - Animal Welfare Act of August 24, 1966 [Full Text, Summary
    - Public Law 91-579 - Animal Welfare Act Amendments of 1970 [Full Text, Summary]
    - Public Law 94-279 - Animal Welfare Act Amendments of 1976 [Full Text, Summary]
    - Public Law 99-198 - Food Security Act of 1985, Subtitle F - Animal Welfare [Full Text, Summary]
    - Public Law 101-624 - Food, Agriculture, Conservation, and Trade Act of 1990, Section 2503 - Protection of Pets [Full Text, Summary]

- Code of Federal Regulations, Title 9, Chapter 1, Subchapter A - Animal Welfare:

    - Part 1 Definition of Terms
    - Part 2 Regulations
    - Part 3 Standards
    - Part 4 Rules of Practice Governing Proceedings under the Animal Welfare Act

- Final Rules: Animal Welfare; 9 CFR Parts 1 and 2. *Federal Register*, Vol. 54, No. 168, August 31, 1989, P. 36112-36163. [Full Text, Summary]

- Final Rule: Animal Welfare; Standards; 9 CFR Part 3. *Federal Register*, Vol. 55, No. 32, February 15, 1991, P. 6426-6505. [Full Text, Summary]

- Final Rule: Random Source Dogs and Cats; 9 CFR Parts 1 and 2. *Federal Register*, Vol. 58, No. 139, July 22, 1993, P. 39124. [Full Text, Summary]

- Final Rule: Correction, Random Source Dogs and Cats; 9 CFR Parts 1 and 2. *Federal Register*, Vol. 58, No. 164, August 26, 1993, P. 45040. [Full Text, Summary]

- Animal Care Policies [Full Text at APHIS/AC website, Summary]

***Animal Welfare Act as Amended* (7 USC, 2131-2156)**
The complete Animal Welfare Act including all amendments (1970, 1976, 1985, 1990) following the 1966 enactment. This version is current through 1996 and can be found in *United States Code*, Title 7, Sections 2131 to 2156. [Full Text]

Public Law 89-544 *Act of August 24, 1966*
Enacted August 24, 1966, Public Law 89-544 is what commonly is referred to as The Animal Welfare Act although that title is not mentioned within the law. It authorizes the Secretary of Agriculture to regulate transport, sale, and handling of dogs, cats, nonhuman primates, guinea pigs, hamsters, and rabbits intended to be used in research or "for other purposes." It requires licensing and inspection of dog and cat dealers and humane handling at auction sales. The complete amended act can be found in *United States Code,* Title 7, Sections 2131-2156. [Full Text]

Public Law 91-579 *Animal Welfare Act of 1970*
Enacted December 24, 1970, Public Law 91-579 expands the list of animals covered by the Act to include all warm-blooded animals determined by the Secretary of Agriculture as being used or intended for use in experimentation or exhibition except horses not used in research and farm animals used in food and fiber research. Exhibitors are incorporated into the act and research facilities are defined. Retail pet stores, state and county fairs, rodeos, purebred dog and cat shows, and agricultural exhibitions are exempt from the Act. The Secretary is directed to develop regulations regarding recordkeeping and humane care and treatment of animals in or during commerce, exhibition, experimentation, and transport. There is also mention of inspections, and appropriate anesthetics, analgesics, and tranquilizers. There are further regulations on dog and cat commerce. [Full Text]

Public Law 94-279 *Animal Welfare Act Amendments of 1976*
Enacted April 22, 1976, Public Law 94-279 is primarily refining previous regulations on animal transport and commerce. "Carrier" and "Intermediate Handler" are defined. Health certification prior to transport of sale is required and must be performed by a veterinarian. Licenses, method of payment, and penalties for violations are discussed. This amendment also introduces and defines "animal fighting ventures" to the Act. Animals used in hunting waterfowl, foxes, etc. are exempt. It is illegal to exhibit or transport via interstate or foreign commerce animals used in fighting ventures such as dogs or roosters. [Full Text]

Public Law 99-198 *Food Security Act of 1985, Subtitle F - Animal Welfare*
Also called "The Improved Standards for Laboratory Animals Act" and enacted December 23, 1985, this section clarifies what is meant by "humane care" by mentioning specifics such as sanitation, housing, and ventilation. It directs the Secretary of Agriculture to establish regulations to provide exercise for dogs and an adequate physical environment to promote the psychological well-being of nonhuman primates. It specifies that pain and distress must be minimized in experimental procedures and that alternatives to such procedures be considered by the principle investigator. It also defines practices that are considered to be painful. No animal can be used in more than one major operative experiment with recovery (exceptions are listed). The establishment of the Institutional Animal Care and Use Committee (IACUC) is introduced with a description of its roles, composition, and responsibilities to the Animal and Plant Health Inspection Service (APHIS). Also included is the formation of an information service at the National Agricultural Library to assist those regulated by the act in prevention of unintended duplication of research, employee training, searching for ways to reduce or replace animal use, and to provide information on how to decrease pain and distress. The final section explains the penalties for release of trade secrets by regulators and the regulated community. [Full Text]

Public Law 101-624 *Food, Agriculture, Conservation, and Trade Act of 1990, Section 2503 - Protection of Pets*
Enacted November 28, 1990, and establishes a holding period for dogs and cats at shelters and other holding facilities before sale to dealers. It requires dealers to provide written certification regarding each animal's background to the recipient. Specific items included on the certificate are mechanisms of enforcement, injunctions, and penalties for violation. [Full Text]

Code of Federal Regulations, Title 9, Chapter 1, Subchapter A - Animal Welfare. Available from: USDA, APHIS/Animal Care, 4700 River Rd., Unit 85, Riverdale, MD 20737-1234.
The current version of the regulations developed by the U. S. Department of Agriculture that specify how to comply with the Animal Welfare Act and its amendments. The section is divided into 4 sections: Definitions, Regulations, Standards, and Rules of Practice Governing Proceedings Under the Animal Welfare Act. The Definitions section describes exactly what is meant by terms used in the legislation. "Animal", for example, specifically excludes rats of the genus *Rattus* and mice of the genus *Mus* as well as birds used in research. The Regulations section includes subparts for licensing, registration, research facilities, attending veterinarians and adequate veterinary care, stolen animals, records, compliance with standards and holding periods, and miscellaneous topics such as confiscation and destruction of animals and access and inspection of records and property. The bulk of the subchapter is the third section which provides standards for specific species or groups of species. Included are sections for cats and dogs, guinea pigs and hamsters, rabbits, nonhuman primates, marine mammals, and the general category of "other warm-blooded animals". Standards include those for facilities and operations, health and husbandry systems, and transportation. The final section sets forth the Rules of Practice applicable to adjudicating administrative proceedings under Section 19 of the Animal Welfare Act. [Full Text at APHIS website]

Federal Register*, Vol. 54, No. 168, August 31, 1989, P. 36112-36163. *Animal Welfare; Final Rules; 9

CFR Parts 1 and 2

Often referred to as the "Preamble" to the Animal Welfare Act amendments of 1985, the explanations of the regulations are used to identify the intent of the regulations published in *Title 9, Code of Federal Regulations*. This issue contains final regulations developed to enact the 1985 amendments to the Animal Welfare Act covering the Definitions and Regulations sections. Extensive commentary is provided to respond to public comments about each of the proposed regulations. Comments and final regulations are provided in many areas including the structure and functions of the Institutional Animal Care and Use Committee; the principal investigator's consideration of alternatives that reduce, refine, or replace animal use; records; licensing; registration; stolen animals; and research facilities. [Full Text]

Federal Register*, Vol. 55, No. 32, February 15, 1991, P. 6426-6505. *Final Rule: Animal Welfare; Standards; Part 3

Often referred to as the "Preamble" to the Animal Welfare Act amendments of 1985, the explanations of the regulations are used to identify the intent of the regulations published in T*itle 9, Code of Federal Regulations*. This issue contains final regulations developed to enact the 1985 amendments to the Animal Welfare Act covering the Standards section. Extensive commentary is provided to respond to public comments about each of the proposed regulations. Comments and final regulations are provided concerning exercise in dogs and psychological well-being in nonhuman primates. [Full Text]

***Federal Register*, Vol. 58, No. 139, July 22, 1993, P. 39124. *Final Rule: Random Source Dogs and Cats*.**

The final rules implementing the 1990 amendment to the Animal Welfare Act and amending the animal welfare regulations by requiring pounds and shelters to hold and care for dogs and cats for at least 5 days (including one weekend day) before providing them to a dealer. Dealers must provide valid certification to anyone acquiring random source dogs and cats from them. Public comments and rationale for the regulatory decisions are discussed. This information updates *Title 9, Code of Federal Regulations, Subpart A, Parts 1 and 2*. [Full Text]

Federal Register*, Vol. 58, No. 164, August 26, 1993, P. 45040. *Final Rule: Correction, Random Source Dogs and Cats.

Revises several sentences in the original final rule. [Full Text]

Animal Care Policies

The policy manual gives policies issued by APHIS/Animal Care that clarify the Animal Welfare Act regulations. Among the topics covered are "Written Narrative for Alternatives to Painful Procedures", "Space and Exercise Requirements for Traveling Exhibitors", and "Annual Report for Research Facilities". Originally issued in April 1997, new policies may be added at any time and included in the manual. [Full Text at APHIS/AC website]

Go to:
AWIC Animal Legislation and Policies Home Page

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The Animal Welfare Information Center
U.S. Department of Agriculture
Agricultural Research Service
National Agricultural Library
10301 Baltimore Ave.
Beltsville, MD 20705-2351

Phone: (301) 504-6212
FAX: (301) 504-7125
E-mail: awic@nal.usda.gov

Disclaimers

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http://www.nal.usda.gov/awic/legislat/usdaleg1.htm